

We Claim:

1. A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising:
administering to a mammalian subject having an abnormal brain region a potassium channel agonist, other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and
administering to the subject simultaneously or substantially simultaneously with the potassium channel agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.
2. The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke, or ischemia.
3. The method of Claim 1, wherein the abnormal brain region is a region of benign or malignant tumor tissue.
4. The method of Claim 1, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levromakalim.
5. The method of Claim 1, wherein said mammal is a human, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit.
6. The method of Claim 1, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.
7. The method of Claim 6, wherein the diagnostic agent is an imaging or contrast agent.
8. The method of Claim 6, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.
9. The method of Claim 1, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic

acid.

10. The method of Claim 6, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

11. The method of Claim 1, wherein administering the potassium channel agonist is by intravenous or intra-arterial infusion or injection.

12. The method of Claim 1, wherein administering the potassium channel agonist is by intracarotid infusion or injection.

13. The method of Claim 1, wherein the potassium channel agonist is administered to the mammalian subject by a bolus injection.

14. The method of Claim 1, wherein the potassium channel agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

15. The method of Claim 14, wherein the potassium channel agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

16. The method of Claim 1, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu\text{g kg}^{-1} \text{min}^{-1}$ for up to about 30 minutes.

17. The method of Claim 16, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu\text{g kg}^{-1} \text{min}^{-1}$.

18. A method of selectively delivering a medicant to an abnormal brain region in a mammalian subject, comprising:

administering to a mammalian subject having an abnormal brain region a potassium channel agonist, other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase potassium flux through a calcium-activated or ATP-sensitive potassium channel in an endothelial cell membrane of a capillary or arteriole delivering blood to cells of the abnormal brain region, whereby the capillary or arteriole is made more permeable to the medicant; and

administering to the subject simultaneously or substantially simultaneously with the potassium channel agonist the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

19. The method of Claim 18, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke, or ischemia.

20. The method of Claim 18, wherein the abnormal brain region is a region of benign or malignant tumor tissue.

21. The method of Claim 18, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levromakalim.

22. The method of Claim 18, wherein said mammal is a human, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit.

23. The method of Claim 18, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

24. The method of Claim 23, wherein the diagnostic agent is an imaging or contrast agent.

25. The method of Claim 23, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

26. The method of Claim 18, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

27. The method of Claim 23, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

28. The method of Claim 18, wherein administering the potassium channel agonist is by intravenous or intra-arterial infusion or injection.
29. The method of Claim 18, wherein administering the potassium channel agonist is by intracarotid infusion or injection.
30. The method of Claim 18, wherein the potassium channel agonist is administered to the mammalian subject by a bolus injection.
31. The method of Claim 18, wherein the potassium channel agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.
32. The method of Claim 31, wherein the potassium channel agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.
33. The method of Claim 18, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu\text{g kg}^{-1} \text{min}^{-1}$ for up to about 30 minutes.
34. The method of Claim 33, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu\text{g kg}^{-1} \text{min}^{-1}$.
35. A method of delivering a medicant to a malignant tumor in a mammalian subject, comprising:
administering to a mammalian subject having a malignant tumor a potassium channel agonist, other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the malignant tumor; and
administering to the subject simultaneously or substantially simultaneously with the potassium channel agonist the medicant, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

36. The method of Claim 35, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levromakalim.

37. The method of Claim 35, wherein the malignant tumor is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

38. The method of Claim 35, wherein the malignant tumor is contained in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said subject.

39. The method of Claim 35, wherein said mammal is a human, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit.

40. The method of Claim 35, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

41. The method of Claim 40, wherein the diagnostic agent is an imaging or contrast agent.

42. The method of Claim 40, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

43. The method of Claim 35, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin,

vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

44. The method of Claim 40, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

45. The method of Claim 35, wherein administering the potassium channel agonist is by intravenous or intra-arterial infusion or injection.

46. The method of Claim 35, wherein the tumor is an intracranial tumor and the potassium channel agonist is administered by intracarotid infusion or injection.

47. The method of Claim 35, wherein the potassium channel agonist is administered to the mammalian subject by a bolus injection.

48. The method of Claim 35, wherein the potassium channel agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

49. The method of Claim 48, wherein the potassium channel agonist is administered to the mammalian subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

50. The method of Claim 35, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about $100 \mu\text{g kg}^{-1} \text{min}^{-1}$ for up to about 30 minutes.

51. The method of Claim 50, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about $15 \mu\text{g kg}^{-1} \text{min}^{-1}$.

52. A method of delivering a medicant to a malignant tumor in a mammalian subject, comprising:
administering to the mammalian subject having a malignant tumor a potassium channel agonist,

other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase potassium flux through a calcium-activated or ATP-sensitive potassium channel in an endothelial cell membrane of a capillary or arteriole delivering blood to malignant cells of the tumor, whereby the capillary or arteriole is made more permeable to the medicant; and

administering to the subject simultaneously or substantially simultaneously with the potassium channel agonist the medicant, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

53. The method of Claim 52, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levcromakalim.

54. The method of Claim 52, wherein the malignant tumor is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

55. The method of Claim 52, wherein the malignant tumor is contained in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said subject.

56. The method of Claim 52, wherein said mammal is a human, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster, or rabbit.

57. The method of Claim 52, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

58. The method of Claim 57, wherein the diagnostic agent is an imaging or contrast agent.

59. The method of Claim 57, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

60. The method of Claim 52, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

61. The method of Claim 57, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

62. The method of Claim 52, wherein administering the potassium channel agonist is by intravenous or intra-arterial infusion or injection.

63. The method of Claim 52, wherein the tumor is an intracranial tumor and the potassium channel agonist is administered by intracarotid infusion or injection.

64. The method of Claim 52, wherein the potassium channel agonist is administered to the mammalian subject by a bolus injection.

65. The method of Claim 52, wherein the potassium channel agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

66. The method of Claim 65, wherein the potassium channel agonist is administered to the mammalian subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

67. The method of Claim 52, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100 $\mu\text{g kg}^{-1} \text{ min}^{-1}$ for up to about 30 minutes.

68. The method of Claim 67, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 15 $\mu\text{g kg}^{-1} \text{ min}^{-1}$.

69. A method of treating a malignant tumor in a human subject, comprising:
administering to a human subject having a malignant tumor a potassium channel agonist, other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the malignant tumor; and
administering to the subject simultaneously or substantially simultaneously with the potassium channel agonist the medicant, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

70. The method of Claim 69, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levcromakalim.

71. The method of Claim 69, wherein the malignant tumor is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

72. The method of Claim 69, wherein the malignant tumor is contained in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said subject.

73. The method of Claim 69, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

74. The method of Claim 73, wherein the diagnostic agent is an imaging or contrast agent.

75. The method of Claim 73, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

76. The method of Claim 69, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

77. The method of Claim 73, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

78. The method of Claim 69, wherein administering the potassium channel agonist is by intravenous or intra-arterial infusion or injection.

79. The method of Claim 69, wherein the tumor is an intracranial tumor and the potassium channel agonist is administered by intracarotid infusion.

80. The method of Claim 69, wherein the potassium channel agonist is administered to the mammalian subject by a bolus injection.

81. The method of Claim 69, wherein the potassium channel agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

82. The method of Claim 69, wherein the potassium channel agonist is administered to the subject at a dose rate of about 0.075 to about 15 $\mu\text{g kg}^{-1} \text{ min}^{-1}$.

83. A method of treating a malignant tumor in a human subject, comprising:
administering to a human subject, having a malignant tumor, a potassium channel agonist, other than bradykinin or a bradykinin analog, under conditions and in an amount sufficient to increase

potassium flux through a calcium-activated or ATP-sensitive potassium channel in an endothelial cell membrane of a capillary or arteriole delivering blood to malignant cells of the malignant tumor, whereby the capillary or arteriole is made more permeable to the medicant; and

administering to the subject simultaneously or substantially simultaneously with the potassium channel agonist the medicant, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

84. The method of Claim 83, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levromakalim.

85. The method of Claim 83, wherein the malignant tumor is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

86. The method of Claim 83, wherein the malignant tumor is contained in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said subject.

87. The method of Claim 83, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

88. The method of Claim 87, wherein the diagnostic agent is an imaging or contrast agent.

89. The method of Claim 87, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

90. The method of Claim 83, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

91. The method of Claim 87, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

92. The method of Claim 83, wherein administering the potassium channel agonist is by intravenous or intra-arterial injection.

93. The method of Claim 83, wherein the tumor is an intracranial tumor and the potassium channel agonist is administered by intracarotid infusion.

94. The method of Claim 83, wherein the potassium channel agonist is administered to the mammalian subject by a bolus injection.

95. The method of Claim 83, wherein the potassium channel agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

96. The method of Claim 83, wherein the potassium channel agonist is administered to the mammalian subject at a dose rate of about 0.075 to about $15 \mu\text{g kg}^{-1} \text{min}^{-1}$.

97. A pharmaceutical composition comprising a combination of a potassium channel agonist, other than bradykinin or a bradykinin analog, formulated in a pharmaceutically acceptable solution together with a medicant for delivery by intravascular infusion or injection into a mammal.

98. The pharmaceutical composition of Claim 97, wherein the solution is formulated to deliver a dose rate of about 0.075 to 1500 micrograms per kilogram body mass in a pharmaceutically acceptable fluid volume over a maximum of about thirty minutes.

99. The pharmaceutical composition of Claim 97, wherein the solution is formulated to deliver a dose rate of about 0.075 to 150 micrograms per kilogram body mass in a pharmaceutically acceptable fluid volume over a period of up to thirty minutes.

100. The pharmaceutical composition of Claim 97, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levcromakalim.

101. The pharmaceutical composition of Claim 97, wherein the medicant is a therapeutic cytotoxic agent, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia-protective agent, anti-trauma agent, anticancer chemotherapeutic agent, or diagnostic agent.

102. The pharmaceutical composition of Claim 101, wherein the diagnostic agent is an imaging or contrast agent.

103. The pharmaceutical composition of Claim 101, wherein the diagnostic agent is a radioactively labeled substance, a gallium-labeled substance, or a contrast agent selected from the group consisting of ferrous magnetic, fluorescent, luminescent, and iodinated contrast agents.

104. The pharmaceutical composition of Claim 97, wherein the medicant is a N-methyl-D-aspartate (NMDA) receptor antagonist, antibiotic, interleukin-2; or transforming growth factor- β , cisplatin, carboplatin, tumor necrosis factor- α , methotrexate, 5-fluorouracil, amphotericin, daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

105. The pharmaceutical composition of Claim 101, wherein the viral vector is an adenovirus-derived vector or herpes simplex virus-derived vector.

106. The pharmaceutical composition of Claim 97, further comprising a buffer solution

pharmaceutically acceptable for intravascular infusion into a mammal.

107. The pharmaceutical composition of Claim 106, wherein the buffer solution is phosphate buffered saline.

108. A kit for enhancing the delivery of a medicant to an abnormal brain region and/or to a malignant tumor, comprising:

a potassium channel agonist, other than bradykinin or a bradykinin analog; and
instructions for using the potassium channel agonist for enhancing the delivery of a medicant to an abnormal brain region or to a malignant tumor.

109. The kit of Claim 108, wherein the potassium channel agonist is NS-1619, 1-EBIO, a guanylyl cyclase activator, a guanylyl cyclase activating protein, minoxidil, pinacidil, cromakalim, or levcromakalim.